UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/692,191 | 10/22/2003 | Pamela Cifra | 13720-105088 | 8424 |

65989 7590 06/15/2007

KING & SPALDING
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-4003

| EXAMINER | |
|---|---|
| ROYDS, LESLIE A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1614 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 06/15/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/692,191 | CIFRA ET AL. | |
| | Examiner | Art Unit | |
| | Leslie A. Royds | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-28,30,31,33-67,73,76-99,105-109 and 111-125* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,24-27,33-35,99,105-108,114-117,119-121 and 123-125* is/are rejected.

7)☒ Claim(s) *123 and 125* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/30/07 & 6/1/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 2-23,28,30,31,36-67,73,76-98,109,111-113,118 and 122.

## DETAILED ACTION

**Claims 1-28, 30-31, 33-67, 73, 76-99, 105-109 and 111-125 are presented for examination.**

A request for continued examination under 37 C.F.R. 1.114, including the fee set forth in 37 C.F.R. 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. 1.114, and the fee set forth in 37 C.F.R. 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 C.F.R. 1.114. Applicant's payment and submission filed March 30, 2007 has been received and entered into the present application. Accordingly, prosecution has been reopened.

Applicant's Information Disclosure Statements (IDS) filed March 30, 2007 (one page) and June 1, 2007 (one page) have each been received and entered into the present application. As reflected by the attached, completed copy of form PTO-1449 (two pages total), the Examiner has considered the cited references.

Claims 1-28, 30-31, 33-67, 73, 76-99, 105-109 and 111-125 are pending. Claims 29, 32, 68-72, 74-75, 99-104 and 110 are cancelled; claims 1, 3, 5, 14-15, 20, 31-32, 34-38, 40-43 and 53 are amended; and claims 115-125 are newly added.

Claims 2-23, 28, 30-31, 36-67, 73, 76-98, 109, 111-113, 118 and 122 are withdrawn from consideration pursuant to 37 C.F.R. 1.142(b). The manner in which claims 28, 109 and 113 (insofar as it depends from newly amended claim 105) have been amended necessitate the withdrawal of such claims from consideration as being directed to non-elected subject matter.

Claims 1, 24-27, 33-35, 99, 105-108, 114-117, 119-121 and 123-125 are under examination as being directed to the elected subject matter.

Applicant's arguments, filed March 30, 2007, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the

instant application.

***Objections to the Claims (New Grounds of Objection)***

Claim 123 is objected to under 37 C.F.R. 1.75 as being a substantial duplicate of present claim 99 insofar as claim 123 is dependent from claim 24. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. Please reference MPEP §706.03(k). Applicant may wish to consider canceling or amending claim 123, since present claim 99 already provides for the use of the zinc compound in the method of claim 24 in a concentration of about 1.0 pM to about 10 mM.

Claim 125 is objected to under 37 C.F.R. 1.75 as being a substantial duplicate of present claim 34 insofar as claim 125 is dependent from claim 24. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. Please reference MPEP §706.03(k). Applicant may wish to consider canceling or amending claim 125, since present claim 34 already provides for the use of the zinc compound in the method of claim 24 in a concentration of about 1.0 pM to about 900 μM.

***Claim Rejections - 35 USC § 103 (New Grounds of Rejection)***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1, 24-27, 33-35, 99, 105-108, 114-117, 119-121 and 123-125 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petrus (U.S. Patent No. 6,573,299; Issued June 2003, Filed September 1999) in view of Uitto ("Connective Tissue Biochemistry of the Aging Dermis. Age-Related Alterations in Collagen and Elastin", *Dermatol Clin*, 1986 Jul; 4(3):433-436; Abstract Only).**

Petrus teaches a method for the treatment of orbital disorders associated with the aging eye, including the improvement of age-related changes to the eyelids, such as dry skin or wrinkles (col.2, l.22-24) by applying a topical composition comprising a penetration enhancer and one or more bio-affecting agents (col.2 l.24-28), such as zinc citrate (col.13, l.21-28, especially col.13, l.25), wherein the bio-affecting agent penetrates the underlying tissue into the vascular network of the orbit via application to the eyelid surface (i.e., meets Applicant's limitation of applying the composition to the face or the furrows or wrinkles of the face as recited in present claims 26 and 107). Petrus further teaches that the composition may also include emollients (i.e., meets Applicant's limitation of a "moisturizer" as recited in present claims 33 and 114; col.14, l.20-24), provided that the inclusion of such an additive does not defeat the objective of the invention (col.14, l.34-35).

Regarding the use of the transitional phrase "consisting essentially of" (claims 1 and 24), the MPEP states at §2111.03, "The transitional phrase 'consisting essentially of' limits the scope of a claim to

the specified materials or steps 'and those that do not materially affect the basis and novel characteristic(s)' of the claimed invention...For the purposes of searching for and applying prior art under 35 U.S.C. §102 and §103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of' will be construed as equivalent to 'comprising'."

Applicant has failed to definitively point out the basic and novel characteristics of the invention. However, taken in its broadest, reasonable interpretation, the basic and novel characteristic of the presently claimed invention must necessarily lie in the fact that the composition must retain efficacy in effecting the increase in elastin content of the tissue to which it is applied. For this reason, the inclusion of any additional elements or steps that affect the function of the claimed active agent (i.e., zinc citrate) would necessarily be excluded from the claimed invention.

If the composition must retain efficacy in effecting the increase in elastin content of the tissue to which it is applied, then the fact that Petrus explicitly teaches the inclusion of additives, such as emollients, that do not defeat the objective of the invention (col.14, l.34-35) is clear evidence that the disclosed additional additive agents are not patentably excluded from the claim language, absent factual evidence to the contrary, because they do not affect the characteristics or properties of the composition taught by the reference.

Though Petrus does not explicitly teach that the application of the disclosed zinc citrate composition effects an increase in the elastin content of the tissue to which it is applied, it is noted that the very administration of the same compound(s) as claimed (i.e., zinc citrate, optionally in combination with a moisturizing compound) topically to the skin of a subject is considered to necessarily have the claimed effect on increasing the elastin content of said tissue, whether recognized by the patentee or not. Products of identical chemical composition cannot exert mutually exclusive properties when administered under

the same circumstances or, in the present case, the same host. In other words, a composition and its effects are inseparable. Please reference MPEP §2112.

The explanation of an effect obtained when using a compound cannot confer novelty on a known process if the skilled artisan was already aware of the occurrence of the desired therapeutic effect. In other words, even if the effect of increasing elastin content of a tissue to which the zinc composition had been applied was not itself recognized as a pharmacological effect of topically applying the claimed zinc citrate composition of Petrus to a patient, such an effect is not considered a new therapeutic application because the known treatment of skin using such a compound was already known and recognized in the prior art. Though mechanisms of action or new properties of a compound are no doubt important contributions to scientific and pharmaceutical development, the assessment of patentability under 35 U.S.C. 102 and/or 35 U.S.C. 103 is based upon the therapeutic applications and effects of the compounds, not the mechanisms and/or properties by which they exert such a therapeutic effect.

The teaching of Petrus to apply the disclosed zinc-containing composition directly to the skin for the improvement of age-related changes to the eyelids, such as dry skin or wrinkles (col.2, l.22-24), necessarily meets Applicant's claimed limitation to the application of the claimed composition to tissue in need of increased elastin content because, as Uitto ("Connective Tissue Biochemistry of the Aging Dermis. Age-Related Alterations in Collagen and Elastin", *Dermatol Clin*, 1986 Jul; 4(3):433-436; Abstract Only) teaches, perturbations in the supramolecular organization of the elastic fiber network as occur with cutaneous aging lead to alterations in the mechanical properties of the skin, as manifested by loose and sagging skin with reduced resilience and elasticity (abstract). In view of such a teaching, the application of the disclosed zinc composition of Petrus to improve the dry and/or wrinkled skin around the eyes is necessarily an area in "need of increased elastin content", whether recognized by the patentee or not, since dry and/or wrinkled skin is necessarily in need of increased elastin to improve elasticity and ameliorate the looseness and sagging of the dry and/or wrinkled skin.

Regarding the claimed dosage amounts of the zinc citrate compound, Petrus expressly teaches that, "The concentration of the bio-affecting agents in the composition can also vary greatly and will be dependent upon many factors, e.g., type, bioavailability, potency, surface area to which it is applied, composition used and the amount of the penetrating agent used." (col.6, l.56-60)

It is obvious from the above teachings that Petrus expressly contemplates variation in the dosage amounts and schedule of the active agent and acknowledges that such a determination would be made in accordance with a variety of factors, each of which would have reasonably commended themselves to one of ordinary skill in the art at the time of the invention and would not have required undue experimentation or have been outside the realm of knowledge generally available to the skilled artisan. Factors that would have been taken into consideration when making such a determination would have included, but would not have been limited to, the age, weight, sex, diet and medical condition of the patient, severity of the disease, route of administration, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the dosage regimen that would have actually been employed would have been expected to vary widely and, in the absence of evidence to the contrary, would not have been inconsistent with that which is presently claimed.

In addition, the concentration of the active ingredient is a result-effective variable, i.e., a variable that achieves a recognized result, and, therefore, the determination of the optimum of workable dosage range would be well within the practice of routine experimentation by the skilled artisan, absent factual evidence to the contrary, and, further, absent any evidence demonstrating a patentable difference between the compositions used and the criticality of the amount(s).

*Response to Applicant's Arguments*

Applicant presents arguments in response to the previous grounds of rejection set forth under 35

U.S.C. 103(a) over Petrus in view of Riordan and Ogle. However, insofar as the claims have been amended and a new ground of rejection is presented *supra*, such remarks will not be further considered herein, with the exception of Applicant's remarks regarding the non-obviousness of the claimed dosage amounts, which are germane to the newly presented ground of rejection set forth above.

Applicant traverses the conclusion that the claimed dosage amounts are obvious in view of the teachings of Petrus, relying upon Examples 1 and 9 of the instant specification in support of the fact that the presently claimed ranges are specific to the claimed effect in increasing elastin content such that doses of zinc that are either too low or too high do not result in the claimed effect on elastin and may, in fact, result in undesirable effects, such as increased sloughing or irritation and/or increased elastase activity.

Applicant's traversal has been fully and carefully considered in its entirety, but fails to be persuasive.

Applicant alleges that the presently claimed dosage amounts are non-obvious over the prior art because the claimed ranges of zinc citrate at doses lower than or higher than those that are claimed demonstrate undesirable side effects, such as increased sloughing or irritation and/or increased elastase activity. While such results of Examples 1 and 9 of the instant specification (those upon which Applicant relies to demonstrate non-obviousness) have been carefully and closely considered, it remains that Applicant's experimental data is solely limited to (1) directed to the use of zinc acetate in varying concentrations and its effect on elastase activity and (2) only show the inhibition of elastase at concentrations of (0.01M)-(0.75M), which corresponds to 10 μM-750 μM, whereas the presently claimed subject matter encompasses unspecified, but "elastin-increasing effective amounts" (see, e.g., claim 24), 1.0 pM to about 900 μM (see, e.g., claim 34), 100 pM to about 500 μM (see, e.g., claim 35), 1.0 pM to about 10 mM (see, e.g., claim 99), or 1.0 pM to about 1.0 mM (see, e.g., claim 124). In other words, the administration of zinc acetate for increasing elastin, where elastase activity is only inhibited in amounts of 0.01-0.75 M, which is equivalent to 10-750 μM, clearly fails to be commensurate in scope with what is

presently claimed. Accordingly, the experimental data does not support the concept of non-obvious dosage amounts over the full scope of the presently claimed subject matter, particularly when Petrus expressly notes that an effective amount of the active agent will necessarily vary depending upon many factors, and, therefore, the disclosed concentrations do not restrict the exemplary amounts taught by the reference.

Further, it remains that the proffered results do not provide a basis for concluding that the claimed subject matter would not have been obvious because the results are limited to a distinctly different zinc salt (i.e., zinc acetate versus zinc citrate) and only show inhibition of elastase activity in the specific range of 0.1-0.75 M, while the claims subject to this rejection encompass the use of zinc citrate in varying amounts of, e.g., "elastin-increasing effective amounts" (see, e.g., claim 24), 1.0 pM to about 900 μM (see, e.g., claim 34), 100 pM to about 500 μM (see, e.g., claim 35), 1.0 pM to about 10 mM (see, e.g., claim 99), or 1.0 pM to about 1.0 mM (see, e.g., claim 124), that have not been correlated in any way to the amounts or zinc compound tested to show that the experimental data is supportive of the non-obviousness of the claimed subject matter. Further, it has not been argued or demonstrated on the record that the results obtained with the exemplified combination would have been exemplary of the same or substantially similar results that would have been expected to occur over the entire scope of the claimed subject matter.

In this regard, MPEP §2144.08(II)(B) is relied upon and reads, in-part: "When considering whether proffered evidence is commensurate in scope with the claimed invention, Office personnel should not require the Applicant to show unexpected results over the entire range of properties possessed by a chemical compound or composition. See, e.g., *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Evidence that the compound or composition possesses superior and unexpected properties in one of a spectrum of common properties can be sufficient to rebut a *prima facie* case of obviousness. Id. For example, a showing of unexpected results for a single member of a claimed

subgenus, or a narrow portion of a claimed range would be sufficient to rebut a *prima facie* case of obviousness if a skilled artisan 'could ascertain a trend in the exemplified data that would allow him to reasonably extend the probative value thereof.' *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980) **(Evidence of the unobviousness of a broad range can be proven by a narrower range when one skilled in the art could ascertain a trend that would allow him to reasonably extend the probative value thereof.)** But see, *In re Grasselli*, 713 F.2d at 743, 218 USPQ at 778 (Evidence of superior properties for sodium containing composition insufficient to establish the non-obviousness of broad claims for a catalyst with 'an alkali metal' where it was well known in the catalyst art that different alkali metals were not interchangeable and Applicant had shown unexpected results only for sodium containing materials); *In re Greenfield*, 571 F.2d 1185, 1189, 197 USPQ 227, 230 (CCPA 1978) (Evidence of superior properties in one species insufficient to establish the nonobviousness of a subgenus containing hundreds of compounds); *In re Lindner*, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972) (one test not sufficient where there was no adequate basis for concluding the other claimed compounds would behave the same way)." (emphasis added)

Here, just as a single point in space fails to define a line, the results demonstrated for the exemplified combination in the exemplified amounts would be insufficient to establish the non-obviousness of the entirety of the presently claimed dosage amounts of the claimed zinc compound (i.e., zinc citrate) absent any concrete evidence or scientifically sound reasoning as to why these other embodiments would have been reasonably expected to demonstrate the same effect. In other words, Applicant has not provided any objective evidence, scientific reasoning or persuasive argument on the record to provide an adequate basis for concluding that exemplary data in the instant specification was somehow probative of the same (or at least substantially similar) effect using the elected subject matter. In short, the evidence is, respectfully, insufficient to be supportive of nonobviousness of the claimed dosage amounts.

In view of the foregoing, when all of the evidence is considered, the totality of the evidence of nonobviousness fails to outweigh the evidence of obviousness as set forth *supra*.

Applicant is further reminded that should he rely upon the fact that a particular amount of the active agent is critical to the invention, Applicant must make an objective showing that the claimed range achieves unexpected results relative to the prior art range and that the unexpected results demonstrate a marked improvement over that achieved using the amounts of the prior art such that the difference shown in actually a difference in kind and not just a difference in degree [*In re Waymouth*, 499 F.2d 1273, 1276, 182 USPQ 290, 293 (CCPA 1974)]. Furthermore, Applicant is further advised that should he rely upon unexpected results to patentably distinguish over the prior art, the present claims must be limited to that embodiment which is, in fact, unexpected.

For these reasons, rejection of claims 1, 24-27, 33-35, 99, 105-108, 114-117, 119-121 and 123-125 remains proper under 35 U.S.C. 103(a) and is **maintained**.

### *Conclusion*

Rejection of claims 1, 24-27, 33-35, 99, 105-108, 114-117, 119-121 and 123-125 is proper and is **maintained**.

Claims 2-23, 28, 30-31, 36-67, 73, 76-98, 109, 111-113, 118 and 122 are **withdrawn** from consideration pursuant to 37 C.F.R. 1.142(b).

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leslie A. Royds
Patent Examiner
Art Unit 1614

June 4, 2007

Ardin H. Marschel 6/8/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER